tumor necrosis factors, colony-stimulating factors, kallikrein, lysozyme, fibronectin, insulin-like growth factors, epidermal growth factor, fibroblast growth factors, platelet-derived growth factor, nerve growth factor, hepatocyte growth factor, vasculogenesis factors and anti-vasculogenesis factors.

REMARKS

Reconsideration and withdrawal of the rejection in the outstanding Office Action are respectfully requested in view of the foregoing amendments and the following remarks.

Summary of Status of Amendments and Office Action

In the present amendment, claims 1-5, 10, 17 and 22 are amended. Therefore, claims 1-24 are pending in the application, with claims 1-4 and 13-16 being independent.

In the Office Action mailed February 20, 2003, claims 1-24 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

Claims 1-6, 8, 10-17, 20, 23 and 24 are rejected under 35 U.S.C. § 102(b) as anticipated by Samaritani et al.

Claims 1, 7, 13 and 19 are rejected under 35 U.S.C. § 102(b) as anticipated by Bjorn et al.

Claims 9, 21 and 22 are rejected under 35 U.S.C. § 103(a) over Samaritani et al. in view of Shigehara et al.

Claim 18 is rejected under 35 U.S.C. § 103(a) over Samaritani et al. in view of Morita et al.

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Response to 112, second paragraph Rejections

In the Office Action, claims 1-24 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite. The Office Action alleges that the phrase water-soluble, nonionic, organic binder is unclear. In response, Applicants have amended the language to nonionic, organic, water-soluble binder, to make it even more clear. Applicants have also amended claims 10 and 22 as suggested by the Office Action to delete the noted typographical error.

Reconsideration and withdrawal of these rejections is respectfully requested in light of these amendments.

Response to 102(b) Rejections

In the Office Action, claims 1-6, 8, 10-17, 20, 23 and 24 are rejected under 35 U.S.C. § 102(b) as anticipated by Samaritani et al. The Office Action asserts that Samaritani teaches a method for stabilization of a physiologically active peptide in a process of preparing a powder containing a physiologically active peptide, wherein the method comprises adding to the aqueous liquid at least one compound selected from mannitol. The Office Action also asserts that Samaritani teaches a method of stabilization of a physiologically active peptide, wherein the powder is made up of particles comprising a physiologically active peptide and mannitol in a weight proportion of 1:1 to 1:50. The Office Action asserts that Samaritani teaches a method of preparing a powder containing a physiologically active peptide, wherein the particles further comprise 6 parts by weight of a nonionic, organic, water-soluble binder. The Office Action also asserts that Samaritani teaches a method of preparing a powder containing a physiologically

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active peptide for which the drying is performed by lyophilization. Finally, the Office Action asserts that Samaritani teaches a method of preparing a powder containing a physiologically active peptide, wherein the physiologically active peptide is human growth hormone.

In response, Applicants note that Samaritani teaches a method to increase the stabilization of hGH for long term storage. Applicants, on the other hand, have developed a method for stabilizing a peptide during the preparation of a powder containing the peptide. This stabilization of the peptide during powder formation is important in the production of peptide-containing powder, and is not taught or suggested in Samaritani. Moreover, Samaritani teaches the importance of using saccharose as a stabilizing agent.

The currently claimed method recites the "drying [of] an aqueous liquid containing the physiologically active peptide, wherein the method comprises adding to the aqueous liquid at least one compound selected from the group of a nonionic surfactant, a nonionic, organic, water soluble binder, hydrogentaed lecithin, and mannitol" (emphasis added). In contrast, Samaritani teaches the drying of a solution containing saccharose and hGH. Saccharose is neither a nonionic surfactant, a nonionic, organic, water soluble binder, hydrogentaed lecithin, or mannitol. Therefore, Samaritani does not disclose every limitation of the claimed method and cannot anticipate the claims.

Further, although Samaritani does disclose use of mannitol with a physiologically active peptide, it does not discuss whether mannitol also stabilized the resultant powder. Thus, Samaritani could not be held to be suggesting the use of mannitol for stabilization as the entirety of the teaching is directed to saccharose, and mannitol's properties are not discussed.

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For these reasons, Applicants respectfully request that the Examiner withdraw the rejection of claims 1-6, 8, 10-17, 20, 23 and 24 are rejected under 35 U.S.C. § 102(b) as anticipated by Samaritani et al.

In the Office Action, claims 1, 7, 13 and 19 are rejected under 35 U.S.C. § 102(b) as anticipated by Bjorn et al. The Office Action asserts that Bjorn teaches a method for stabilization of a physiologically active peptide in a process of preparing a powder containing the physiologically active peptide, wherein the method comprises adding to the aqueous liquid at least one compound selected from a nonionic surfactant polysorbate or poloxamer. In response, Applicants note that Bjorn does not teach a method of using a non-ionic detergent, polysorbate or poloxamer, alone, but instead teaches its use in combination with a certain amino acid sequence or peptide having specific features. Further, Bjorn does not teach or suggest stabilizing a physiologically active peptide by using the surfactant and the specific amino acid sequence or peptide having specific features during the powder formation process. Therefore, because Bjorn does not teach all of the claimed limitations, it can not anticipate the claimed invention.

For these reasons, Applicants respectfully request that the Examiner withdraw the rejection of claims 1, 7, 13 and 19 under 35 U.S.C. § 102(b) as anticipated by Bjorn et al.

Response to 103(a) Rejections

In the Office Action, claims 9, 21 and 22 are rejected under 35 U.S.C. § 103(a) over Samaritani et al. in view of Shigehara et al. The Office Action asserts that Shigehara teaches

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average particle sizes of 1-10 μm and a vasculogenesis factor composition containing a physiologically active peptide.

Applicants note that in parent application 09/810,483, a rejection of the composition claims was made using the same argument. In that case, Applicants noted that

> Contrary to the statements in the Office Action, Shigehara is directed to a pharmaceutical composition containing a pyridazinone derivative. Shigehara merely states at col. 7, lines 59-66 that an "inhalant may be formulated by dissolving the compound of the present invention ... or may be administered to the respiratory airway in the form of a fine powder." Shigehara then further comments in a general manner in col. 8, lines 1-5 that "[s]uch an inhalant may be used, if necessary, in combination with other antiasthmatic agent or bronchodilator, such as Salbutamol, Ephedrin, Theophyline, Corticosteroid or ACTH."
>
> It is clear that in these passages, Shigehara simply teaches the use of his pyridazinone derivative inhalant "in combination with" one of the other such agents. Shigehara does not teach the use of a powder which contains only peptides and inert ingredients, much less an inhalant. In particular, his reference to ACTH, a peptide, in the passage does not indicate explicitly or implicitly the use of an inhalant "containing ACTH," for inhalation is not a common way of administration of a peptide. Shigehara does not provide any reference to administering a peptide by inhalation or a single example of an inhalant containing a peptide. Thus, the passage in Shigehara does not suggest any use of a powder containing a peptide.
>
> Shigehara, therefore, does not motivate a person of ordinary skill in the art to combine its teachings with Samaritani for preparing an inhalable peptide composition. In view of Shigehara's failure to teach an inhalable peptide, and the lack of suggestion within Shigehara to combine its teachings with Samaritani, Applicants respectfully request reconsideration and withdrawal of the rejection.

In response to these arguments, the Examiner withdrew the rejection of the claims in issue under 35 U.S.C. § 103(a). Applicants respectfully submit that this rejection of claims 9, 21 and 22 is also improper for the same reasons noted in the parent application, and should be withdrawn.

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In the Office Action, claim 18 is rejected under 35 U.S.C. § 103(a) over Samaritani et al. in view of Morita et al. The Office Action asserts that Morita teaches the use of the water-soluble, nonionic cellulose derivative hydroxypropylmethylcellulose. In response, Applicants wish to point out to the Examiner that the subject matter of the claims is a methods of making a powder. In contrast, Morita discloses a method of making a tablet. Furthermore, Morita teaches covering this tablet with hydroxypropylmethylcellulose to protect the tablets contents from light. The Office Action fails to provide a viable reason why one of skill in the art would use a tablet covering agent in the mixing of a powder. The teachings of Morita are in a nonanalogous art, and one of ordinary skill would not be motivated to use hydroxypropylmethylcellulose in the manufacturing process of a powder, especially where it is taught as a coating agent.

For this reason, Applicants respectfully submit that they have traversed the Office Actions rejections under 35 U.S.C. § 103(a), and respectfully request that the Examiner withdraw the rejections of claims 9, 18, 21 and 22.

CONCLUSION

For the foregoing reasons, it is believed that all of the claims in this application are in condition for allowance, which action is respectfully requested. In summary, Applicants have amended the objected claim language, and replaced them with new claims 33-54 and have also addressed the Examiner's art based rejections and pointed to the fallacies contained within them, as discussed above. Thus it is believed that all of the claims are in condition for allowance, which action is respectfully requested.

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If the Examiner has any questions, or wishes to discuss this matter, the Examiner is respectfully invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
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MARKED-UP COPY OF AMENDED CLAIM

1. (Amended) A method of stabilization of a physiologically active peptide in a process of preparing a powder containing the physiologically active peptide by drying an aqueous liquid containing the physiologically active peptide, wherein the method comprises adding to the aqueous liquid at least one compound selected from the group [consisting] of a nonionic surfactant, a [water-soluble,] nonionic, organic, water soluble binder, hydrogentaed lecithin, and mannitol.

2. (Amended) A method of stabilization of a physiologically active peptide in a process of preparing a powder containing the physiologically active peptide by drying an aqueous liquid containing the physiologically active peptide, wherein the method comprises adding to the aqueous liquid mannitol and at least one compound selected from the group [consisting] of a nonionic surfactant; a [water-soluble,] nonionic, organic, water soluble binder and hydrogentaed lecithin.

3. (Amended) A method of stabiliaation of a physiologically active peptide in a process of preparing a powder containing the physiologically active peptide by drying an aqueous liquid containing the physiologically active peptide, wherein the method comprises adding to the aqueous liquid at least one component selected from the group [consisting] of a nonionic surfactant in an amount of 0.01-0.5% by weight, a [water-soluble,] nonionic, organic, water soluble binder in an amount of 0.01-0.1% by weight, hydrogentaed lecithin, and 1-50 parts by weight mannitol per one part by weight of the physiologically active peptide.

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4. (Amended) A method of stabilization of a physiologically active peptide in a process of preparing a powder containing the physiologically active peptide by drying an aqueous liquid containing the physiologically active peptide, wherein the method comprises adding to the aqueous liquid 1-50 parts by weight mannitol per one part by weight of the physiologically active peptide and at least one component selected from the group [consisting] of a nonionic surfactant in an amount of 0.01-0.5% by weight, a [water-soluble,] nonionic, organic, water soluble binder in an amount of 0.01-0.1% by weight, and hydrogentaed lecithin.

5. (Twice Amended) The method claim 1 wherein the [water-soluble,] nonionic, organic, water-soluble binder is selected from the group [consisting] of polyvinylpyrrolidone, a water-soluble, nonionic cellulose derivative, and polyvinylalcholol.

10. (Twice Amended) The method of claim 1 wherein the physiologically active peptide is selected from the group [consisting] of growth hormones, insulins, calcitonins, erythropoietin, glucagon, somatostatin, somatostatin derivatives, interferons, interleukins, superoxide[,] dismutase, urokinase, proteases, tumor necrosis factors, colony-stimulating factors, kallikrein, lysozyme, fibronectin, insulin-like growth factors, epidermal growth factor, fibroblast growth factors, platelet-derived growth factor, nerve growth factor, hepatocyte growth factor, vasculogenesis factors and anti-vasculogenesis factors.

17. (Twice Amended) The method for preparation of a powder containing a physiologically active peptide of claim 13 wherein the [water-soluble,] nonionic, organic, water-

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soluble binder is selected from the group [consisting] of polyvinylpyrrolidone, a water-soluble, nonionic cellulose derivative, and polyvinylalcholol.

22. (Twice Amended) The method for preparation of a powder containing a physiologically active peptide of claim 13 wherein the physiologically active peptide is selected from the group [consisting] of growth hormones, insulins, calcitonins, erythropoietin, glucagon, somatostatin, somatostatin derivatives, interferons, interleukins, superoxide[,] dismutase, urokinase, proteases, tumor necrosis factors, colony-stimulating factors, kallikrein, lysozyme, fibronectin, insulin-like growth factors, epidermal growth factor, fibroblast growth factors, platelet-derived growth factor, nerve growth factor, hepatocyte growth factor, vasculogenesis factors and anti-vasculogenesis factors.

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